Annexure-1

http://www.cancer.org/docroot/ETO/content/ETO_1_4X_What_Is_Antiangiogenesis_Therapy.asp?sitearea=ETO

What Is Anti-angiogenesis Treatment?

Angiogenesis is the creation of new blood vessels. The term comes from 2 Greek words: **angio**, meaning "blood vessel," and **genesis**, meaning "beginning."

Normally, this is a healthy process. As the human body grows and develops, it needs to make new blood vessels to get blood to all of its cells. As adults, we don't have quite the same need for making new blood vessels, but there are times when angiogenesis is still important. New blood vessels, for instance, help the body heal wounds and repair damaged body tissues.

But in a person with cancer, this same process creates new, very small blood vessels that provide a tumor with its own blood supply and allow it to grow.

Anti-angiogenesis is a form of targeted therapy that uses drugs or other substances to stop tumors from making new blood vessels. Without a blood supply, tumors can't grow.

Revised: 11/30/2006

Annexure-2

Antitumor effect of arterial administration of a medium-chain triglyceride solution of an angiogenesis inhibitor, TNP-470, in rabbits bearing VX-2 carcinoma.

Yanai S, Okada H, Saito K, Kuge Y, Misaki M, Ogawa Y, Toguchi H.

DDS Research Laboratories, Takeda Chemical Industries, Ltd., Osaka, Japan.

Pharm Res. 1995 May;12(5):653-7

Using rabbits bearing VX-2 carcinoma on the inner side of the leg, we examined the antitumor activity of a medium-chain triglyceride (MCT) solution of an angiogenesis inhibitor, TNP-470 (AGM-1470, 6-O-(N-chloroacetylcarbamoyl)-fumagillol), following administration into the femoral artery feeding the tumor. The MCT solution of TNP-470 (1 and 5 mg) strongly suppressed tumor growth following a single intra-arterial (i.a.) injection 2 or 3 weeks after tumor inoculation. Moreover, remarkable regression of well-developed tumors, those 4 weeks after inoculation, was obtained by i.a. injection of the MCT solution containing 20 mg of TNP-470 without any influence on body weight. The antitumor effects were potentiated by coadministration of doxorubicin or mitomycin C (MMC) in the solution or microspheres containing MMC. In a shell-less chorioallantoic membrane (CAM) assay, angiogenesis was inhibited when a droplet of the MCT solution containing 25 micrograms of TNP-470 was placed on the CAM for 2 days, suggesting that the prolonged antitumor effect resulted from the inhibition of tumor neovascularization by sustained drug release from the preparation. These results indicate that i.a. injection of the MCT solution of TNP-470 is promising for treating well-developed tumors.

PMID: 7479548 [PubMed – indexed for MEDLINE]

Annexure-3

Efficacy of hyperthermia and polyunsaturated fatty acids on experimental carcinoma.

Kokura S, Yoshikawa T, Kaneko T, Iinuma S, Nishimura S, Matsuyama K, Naito Y, Yoshida N, Kondo M.

First Department of Internal Medicine, Kyoto Prefectural University of Medicine, Kamigyo-ku, Japan.

Cancer Res. 1997 Jun 1;57(11):2200-2

We investigated the efficacy of hyperthermia and gamma-linolenic acid on experimental carcinoma. This study focused on polyunsaturated fatty acids that are substrates for free radical reactions. Oleic acid, linolenic acid, alpha-linolenic acid, or gamma-linolenic acid was injected into the arteries feeding AH109A carcinoma implanted into rat hind limbs. Among these, gamma-linolenic acid had the greatest effect on tumor tissue lipid peroxidation and demonstrated an antitumor effect. Consequently, gamma-linolenic acid injection into the feeding artery of a tumor was performed immediately prior to hyperthermia. This combination therapy induced a high level of lipid peroxidation in tumor tissue and a significant antitumor effect. Hyperthermia combined with gamma-linolenic acid produces free radical reactions by increasing the radical reaction substrate and may be an effective anticancer modality.

PMID: 9187121 [PubMed – indexed for MEDLINE]

Annexure-4

Items 1 - 12 of 12

One page.

☐ **1:** Related Articles, Links

Zerp SF, Vink SR, Ruiter GA, Koolwijk P, Peters E, van der Luit AH, de Jong D, Budde M, Bartelink H, van Blitterswijk WJ, Verheij M.

Alkylphospholipids inhibit capillary-like endothelial tube formation in vitro: antiangiogenic properties of a new class of antitumor agents.

Anticancer Drugs. 2008 Jan;19(1):65-75.

PMID: 18043131 [PubMed - indexed for MEDLINE]

☐ **2:**Related Articles, Links

Aoki S, Cho SH, Ono M, Kuwano T, Nakao S, Kuwano M, Nakagawa S, Gao JQ, Mayumi T, Shibuya M, Kobayashi M.

Bastadin 6, a spongean brominated tyrosine derivative, inhibits tumor angiogenesis by inducing selective apoptosis to endothelial cells.

Anticancer Drugs. 2006 Mar;17(3):269-78.

PMID: 16520655 [PubMed - indexed for MEDLINE]

☐ **3:** Related Articles, Links

Keller ET.

Metastasis suppressor genes: a role for raf kinase inhibitor protein (RKIP).

Anticancer Drugs. 2004 Aug;15(7):663-9. Review.

PMID: 15269597 [PubMed - indexed for MEDLINE]

☐ **4:** Related Articles, Links

Newcomb EW.

Flavopiridol: pleiotropic biological effects enhance its anti-cancer activity.

Anticancer Drugs. 2004 Jun;15(5):411-9. Review.

PMID: 15166614 [PubMed - indexed for MEDLINE]

☐ **5:** Related Articles, Links

Brooks TD, Wang SW, Brünner N, Charlton PA.

XR5967, a novel modulator of plasminogen activator inhibitor-1 activity, suppresses tumor cell invasion and angiogenesis in vitro.

Anticancer Drugs. 2004 Jan;15(1):37-44.

PMID: 15090742 [PubMed - indexed for MEDLINE]

☐ **6:** Related Articles, Links

Gingras D, Boivin D, Deckers C, Gendron S, Barthomeuf C, Béliveau R.

Neovastat--a novel antiangiogenic drug for cancer therapy.

Anticancer Drugs. 2003 Feb;14(2):91-6. Review.

PMID: 12569294 [PubMed - indexed for MEDLINE]

☐ **7:** Related Articles, Links

Xu XC.

COX-2 inhibitors in cancer treatment and prevention, a recent development.

Anticancer Drugs. 2002 Feb;13(2):127-37. Review.

PMID: 11901304 [PubMed - indexed for MEDLINE]

☐ **8:** Related Articles, Links

Mazar AP.

The urokinase plasminogen activator receptor (uPAR) as a target for the diagnosis and therapy of cancer.

Anticancer Drugs. 2001 Jun;12(5):387-400. Review.

PMID: 11395568 [PubMed - indexed for MEDLINE]

☐ **9:** Related Articles, Links

Drabek K, Pesić M, Piperski V, Ruzdijić S, Medić-Mijacević L, Pietrzkowski Z, Rakić L.

8-Cl-cAMP and tiazofurin affect vascular endothelial growth factor production and glial fibrillary acidic protein expression in human glioblastoma cells.

Anticancer Drugs. 2000 Oct;11(9):765-70.

PMID: 11129740 [PubMed - indexed for MEDLINE]

☐ **10:** Related Articles, Links

Zareneyrizi F, Yang DJ, Oh CS, Ilgan S, Yu DF, Tansey W, Liu CW, Kim EE, Podoloff DA.

Synthesis of [99mTc]ethylenedicysteine-colchicine for evaluation of antiangiogenic effect.

Anticancer Drugs. 1999 Aug;10(7):685-92.

PMID: 10507319 [PubMed - indexed for MEDLINE]

☐ **11:** Related Articles, Links

Maier JA, Delia D, Thorpe PE, Gasparini G.

In vitro inhibition of endothelial cell growth by the antiangiogenic drug AGM-1470 (TNP-470) and the anti-endoglin antibody TEC-11.

Anticancer Drugs. 1997 Mar;8(3):238-44.

PMID: 9095328 [PubMed - indexed for MEDLINE]

☐ **12:** Related Articles, Links

Oikawa T, Hasegawa M, Morita I, Murota S, Ashino H, Shimamura M, Kiue A, Hamanaka R, Kuwano M, Ishizuka M, et al.

Effect of 15-deoxyspergualin, a microbial angiogenesis inhibitor, on the biological activities of bovine vascular endothelial cells.

Anticancer Drugs. 1992 Jun;3(3):293-9.

PMID: 1381973 [PubMed - indexed for MEDLINE]

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